PLOUËT et al. Appl. No. 10/566.679

Atty Ref.: 1487-28 January 30, 2008

Amendment

AMENDMENTS TO THE CLAIMS:

Amend the claims as follows:

Claims 1-9. (Cancelled)

10. (Currently Amended) A method for the treatment:

- of pathologies requiring the inhibition of endothelial proliferation, in particular

within the framework of the following pathologies; age-related macular degeneration.

diabetic retinopathy, rheumatoid arthritis, angiomas, angiosarcomas, in particular

Castelman's disease and Kaposi's sarcoma, or

- of pathologies requiring the inhibition of endothelial activation, in particular

within the framework of the following pathologies: allograft and xenograft rejection,

acrocyanosis, scleroderma, or within the framework of the preparation of grafts between

collection and transplantation,

said method comprising the administration to a person in need of said inhibition

of a pharmaceutically acceptable amount:

- of a protein characterized in that it comprises or is constituted by:

the NOV protein, represented by the sequence SEQ ID NO: 2, or

a fragment of this protein, providing that this fragment exhibits an angiogenesis-

inhibiting activity, said fragment comprising in particular approximately 40 to

approximately 180 amino acids, and being in particular represented by one of the

following sequences SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 or

SEQ ID NO: 12, or any sequence derived from the sequence SEQ ID NO: 2 or from a

- 2 -

PLOUËT et al.

Appl. No. 10/566,679 Attv Ref.: 1487-28

January 30, 2008 Amendment

fragment defined above, in particular by substitution, deletion or addition of one or more

amino acids, providing that this derived sequence exhibits an angiogenesis-inhibiting

activity, or any sequence homologous to the sequence SEQ ID NO: 2 or to a fragment

defined above, preferably having a homology of at least approximately 80%, and in

particular 85%, with the region comprised between the amino acids in positions (33) and

(338) of the sequence SEQ ID NO: 2, providing that this homologous sequence exhibits

an angiogenesis-inhibiting activity,

- or of a nucleotide sequence characterized in that it comprises or is constituted

by a nucleotide sequence coding:

either for the NOV protein as defined above,

or for a fragment of the NOV protein as defined above.

or for a sequence derived from the NOV protein as defined above,

or for a sequence homologous to the NOV protein as defined above.

said nucleotide sequence corresponding in particular to the nucleotide sequence

SEQ ID NO: 1 coding for SEQ ID NO: 2, or to the sequence SEQ ID NO: 3 coding for

SEQ ID NO: 4, or to the sequence SEQ ID NO: 5 coding for SEQ ID NO: 6, or to the

sequence SEQ ID NO: 7 coding for SEQ ID NO: 8, or to the sequence SEQ ID NO: 9

coding for SEQ ID NO: 10. or to the sequence SEQ ID NO: 11 coding for SEQ ID NO:

12.

or of an anti-idiotypic antibody of the NOV protein.

- 3 -

PLOUËT et al. Appl. No. 10/566,679 Atty Ref.: 1487-28

January 30, 2008 Amendment

11. (Previously Presented) The method according to claim 10, comprising the

administration of a pharmaceutically acceptable amount of a protein characterized in

that it comprises or is constituted by:

the NOV protein, represented by the sequence SEQ ID NO: 2, or a

fragment of this protein, providing that this fragment exhibits an angiogenesis-inhibiting

activity, said fragment comprising in particular approximately 40 to approximately 180

amino acids, and being in particular represented by one of the following sequences

SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 12, or

any sequence derived from the sequence SEQ ID NO: 2 or from a fragment defined

above, in particular by substitution, deletion or addition of one or more amino acids,

providing that this derived sequence exhibits an angiogenesis-inhibiting activity, or any

sequence homologous to the sequence SEQ ID NO: 2 or to a fragment defined above,

preferably having a homology of at least approximately 80%, and in particular 85%, with

the region comprised between the amino acids in positions (33) and (338) of the

sequence SEQ ID NO: 2, providing that this homologous sequence exhibits an

angiogenesis-inhibiting activity.

12. (Previously Presented) The method according to claim 10, comprising the

administration of a pharmaceutically acceptable amount of a protein characterized in

that it comprises or is constituted by the NOV protein, represented by the sequence

SEQ ID NO: 2.

- 4 -

PLOUËT et al. Appl. No. 10/566,679 Atty Ref.: 1487-28 January 30, 2008

Amendment

13. (Previously Presented) The method according to claim 10, comprising the administration of a pharmaceutically acceptable amount of a protein characterized in that it comprises or is constituted by:

a fragment of the NOV protein, represented by the sequence SEQ ID NO: 2, providing that this fragment exhibits an angiogenesis-inhibiting activity, said fragment comprising in particular approximately 40 to approximately 180 amino acids, and being in particular represented by one of the following sequences SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 10 or SEQ ID NO: 12, or any sequence derived from the sequence SEQ ID NO: 2 or from a fragment defined above, in particular by substitution, deletion or addition of one or more amino acids, providing that this derived sequence exhibits an angiogenesis-inhibiting activity, or any sequence homologous to the sequence SEQ ID NO: 2 or to a fragment defined above, preferably having a homology of at least approximately 80%, and in particular 85%, with the region comprised between the amino acids in positions (33) and (338) of the sequence SEQ ID NO: 2, providing that this homologous sequence exhibits an angiogenesis-inhibiting activity.

14. (Previously Presented) A method for the treatment of cancer, comprising the administration of a pharmaceutically acceptable amount of a protein characterized in that it comprises or is constituted by: a fragment of the NOV protein, represented by the sequence SEQ ID NO: 2, providing that this fragment exhibits an angiogenesis-inhibiting activity, said fragment comprising in particular approximately 40 to

PLOUËT et al. Appl. No. 10/566,679 Atty Ref.: 1487-28 January 30, 2008

Amendment

approximately 180 amino acids, and being in particular represented by one of the following sequences SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 12, or ,any sequence derived from the sequence SEQ ID NO: 2 or from a fragment defined above, in particular by substitution, deletion or addition of one or more amino acids, providing that this derived sequence exhibits an angiogenesis-inhibiting activity, or any sequence homologous to the sequence SEQ ID NO: 2 or to a fragment defined above, preferably having a homology of at least approximately 80%, and in particular 85%, with the region comprised between the amino acids in positions (33) and (338) of the sequence SEQ ID NO: 2, providing that this homologous sequence exhibits an angiogenesis-inhibiting activity.

- 15. (Previously Presented) A pharmaceutical composition characterized in that it contains as active ingredient:
- a protein characterized in that it comprises or is constituted by: a fragment of the NOV protein, represented by the sequence SEQ ID NO: 2, providing that this fragment exhibits an angiogenesis-inhibiting activity, said fragment comprising in particular approximately 40 to approximately 180 amino acids, and being in particular represented by one of the following sequences SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 12, or any sequence derived from the sequence SEQ ID NO: 2 or from a fragment defined below, in particular by substitution, deletion or addition of one or more amino acids, providing that this derived sequence exhibits an angiogenesis-inhibiting activity, or any sequence homologous to the sequence SEQ ID

PLOUËT et al. Appl. No. 10/566,679 Atty Ref.: 1487-28

January 30, 2008

Amendment

NO: 2 or to a fragment defined below, preferably having a homology of at least

approximately 80%, and in particular 85%, with the region comprised between the

amino acids in positions (33) and (338) of the sequence SEQ ID NO: 2, providing that $\,$

this homologous sequence exhibits an angiogenesis-inhibiting activity, or

- a nucleotide sequence characterized in that it comprises or is constituted by a

nucleotide sequence coding: either for the NOV protein as defined above, or for a

fragment of the NOV protein as defined above, or for a sequence derived from the NOV

protein as defined above, or for a sequence homologous to the NOV protein as defined

above, said nucleotide sequence corresponding in particular to the nucleotide

sequence SEQ ID NO: 1 coding for SEQ ID NO: 2, or to the sequence SEQ ID NO: 3

coding for SEQ ID NO: 4, or to the sequence SEQ ID NO: 5 coding for SEQ ID NO: 6,

or to the sequence SEQ ID NO: 7 coding for SEQ ID NO: 8, or to the sequence SEQ ID

NO: 9 coding for SEQ ID NO: 10, or to the sequence SEQ ID NO: 11 coding for SEQ ID $\,$

NO: 12, or

- an anti-idiotypic antibody of the NOV protein,

in combination with a pharmaceutically acceptable vector.

16. (Previously Presented) The pharmaceutical composition according to claim

15, characterized in that it contains as active ingredient a protein characterized in that it

comprises or is constituted by: a fragment of the NOV protein, represented by the

sequence SEQ ID NO: 2, providing that this fragment exhibits an angiogenesis-

inhibiting activity, said fragment comprising in particular approximately 40 to

-7-

PLOUËT et al.

Appl. No. 10/566,679 Attv Ref.: 1487-28

January 30, 2008 Amendment

approximately 180 amino acids, and being in particular represented by one of the

following sequences SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 or

SEQ ID NO: 12, or any sequence derived from the sequence SEQ ID NO: 2 or from a

fragment defined above, in particular by substitution, deletion or addition of one or more

amino acids, providing that this derived sequence exhibits an angiogenesis-inhibiting

activity, or any sequence homologous to the sequence SEQ ID NO: 2 or to a fragment

defined above, preferably having a homology of at least approximately 80%, and in

particular 85%, with the region comprised between the amino acids in positions (33) and

(338) of the sequence SEQ ID NO: 2, providing that this homologous sequence exhibits

an angiogenesis-inhibiting activity,

in combination with a pharmaceutically acceptable vector.

17. (Previously Presented) The pharmaceutical composition according to claim

15, characterized in that it contains as active ingredient the sequence SEQ ID NO: 8.

18. (Currently Amended) A method for the treatment:

- of pathologies requiring the inhibition of endothelial proliferation, in particular

within the framework of the following pathologies: age-related macular degeneration.

diabetic retinopathy, rheumatoid arthritis, angiomas, angiosarcomas, in particular

Castelman's disease and Kaposi's sarcoma, or

of pathologies requiring the inhibition of endothelial activation, in particular

within the framework of the following pathologies: allograft and xenograft rejection,

- 8 -

PLOUËT et al. Appl. No. 10/566,679 Atty Ref.: 1487-28 January 30, 2008

Amendment

acrocyanosis, scleroderma, or within the framework of the preparation of grafts between collection and transplantation.

said method comprising the administration to a person in need to said inhibition of a pharmaceutical composition characterized in that it contains as active ingredient:

— a protein characterized in that it comprises or is constituted by: a fragment of the NOV protein, represented by the sequence SEQ ID NO: 2, providing that this fragment exhibits an angiogenesis-inhibiting activity, said fragment comprising in particular approximately 40 to approximately 180 amino acids, and being in particular represented by one of the following sequences SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10 or SEQ ID NO: 12, or any sequence derived from the sequence SEQ ID NO: 2 or from a fragment defined below, in particular by substitution, deletion or addition of one or more amino acids, providing that this derived sequence exhibits an angiogenesis-inhibiting activity, or any sequence homologous to the sequence SEQ ID NO: 2 or to a fragment defined below, preferably having a homology of at least approximately 80%, and in particular 85%, with the region comprised between the amino acids in positions (33) and (338) of the sequence SEQ ID NO: 2, providing that this homologous sequence exhibits an angiogenesis-inhibiting activity, or

– a nucleotide sequence characterized in that it comprises or is constituted by a nucleotide sequence coding: either for the NOV protein as defined above, or for a fragment of the NOV protein as defined above, or for a sequence derived from the NOV protein as defined above, or for a sequence homologous to the NOV protein as defined above, said nucleotide sequence corresponding in particular to the nucleotide sequence

PLOUËT et al. Appl. No. 10/566,679

Atty Ref.: 1487-28

January 30, 2008 Amendment

SEQ ID NO: 1 coding for SEQ ID NO: 2, or to the sequence SEQ ID NO: 3 coding for

SEQ ID NO: 4, or to the sequence SEQ ID NO: 5 coding for SEQ ID NO: 6, or to the

sequence SEQ ID NO: 7 coding for SEQ ID NO: 8, or to the sequence SEQ ID NO: 9

coding for SEQ ID NO: 10, or to the sequence SEQ ID NO: 11 coding for SEQ ID NO:

12, or

- an anti-idiotypic antibody of the NOV protein,

in combination with a pharmaceutically acceptable vector,

said pharmaceutical composition being administered at a rate of approximately

0.1 to approximately 20 mg/kg/day.

- 10 -